DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

JAN 18 2001

Sidney M. Wolfe, M.D.
Director
Public Citizen Health Research Group
1600 20th Street, NW
Washington, DC 20009-1001

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Re: Docket Nos. 81N-0022 and 76N-052N
Comment Nos. CP19 and CP17, respectively

Dear Dr. Wolfe:

This letter is an interim response to your petition submitted on October 19, 2000, asking the Food and Drug Administration (FDA) to immediately ban all uses of phenylpropanolamine in over-the-counter (OTC) drug products, including use as the active ingredient in appetite suppressants and as a nasal decongestant in cough-cold products. You provided a number of arguments as to why phenylpropanolamine should no longer be considered safe for OTC use and asked that FDA remove it from all OTC drug products as quickly as possible.

As you already know, FDA issued a public health advisory on November 6, 2000 (copy enclosed) to alert consumers and health professionals that the agency is taking steps to remove phenylpropanolamine from all drug products. The first step in that process was a letter sent on November 3, 2000 to the CEO or President of all companies identified as now marketing or having previously manufactured, relabeled, repacked, or distributed a prescription or OTC drug product containing phenylpropanolamine (copy enclosed). In that letter, the agency asked all companies to voluntarily discontinue marketing any drug products containing phenylpropanolamine. The response from industry has been encouraging to date.

The next steps, as stated in the letter, will include rulemaking to classify phenylpropanolamine as nonmonograph (not generally recognized as safe and effective) for OTC use. OTC products sold under New Drug Applications will be handled separately, in accordance with regulations governing these products. We also plan to remove phenylpropanolamine from prescription products. We will complete this work as quickly as possible.

While we did not immediately ban all marketing as you requested, we believe the steps that we are taking will result in a prompt removal of phenylpropanolamine from all products in the marketplace using our administrative procedures and informing the public and health professionals of our actions.

Sincerely yours,

Janet Woodcock, M.D.
Director
Center for Drug Evaluation and Research

Enclosures

81N-0022

LET 114

FOOD AND DRUG ADMINISTRATION

PUBLIC HEALTH ADVISORY

SUBJECT: SAFETY OF PHENYLPROPANOLAMINE

November 6, 2000

The Food and Drug Administration (FDA) is issuing a public health advisory concerning phenylpropanolamine hydrochloride. This drug is widely used as a nasal decongestant (in over-the-counter and prescription drug products) and for weight control (in over-the-counter drug products). FDA is taking steps to remove phenylpropanolamine from all drug products and has requested that all drug companies discontinue marketing products containing phenylpropanolamine.

Phenylpropanolamine has been marketed for many years. A recent study reported that taking phenylpropanolamine increases the risk of hemorrhagic stroke (bleeding into the brain or into tissue surrounding the brain) in women. Men may also be at risk. Although the risk of hemorrhagic stroke is very low, FDA recommends that consumers not use any products that contain phenylpropanolamine.

FDA's Nonprescription Drugs Advisory Committee (NDAC) recently discussed this study and other information on phenylpropanolamine. NDAC determined that there is an association between phenylpropanolamine and hemorrhagic stroke and recommended that phenylpropanolamine not be considered safe for over-the-counter use.

Although this risk of hemorrhagic stroke is very low, FDA has significant concerns because of the seriousness of a stroke and the inability to predict who is at risk. FDA does not consider the conditions for which phenylpropanolamine is used (over-the-counter or by prescription) as justifying the risk of this serious event. Other products are available for use.

In the meantime, consumers can identify over-the-counter cough-cold, nasal decongestant, and weight control products containing this ingredient by looking for "phenylpropanolamine" in the list of active ingredients on the label. Consumers can check with their health care provider or pharmacist to see whether their prescription cough-cold or nasal decongestant product contains phenylpropanolamine. We advise consumers to discuss alternative over-the-counter and prescription products with their health care providers or pharmacists.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

November 3, 2000

Dear CEO or President:

This letter concerns drug products containing phenylpropanolamine and its salts marketed by prescription or over-the-counter (OTC), which are now or have previously been manufactured, relabeled, repacked, or distributed by your firm. Phenylpropanolamine is currently available by prescription and OTC as a nasal decongestant, and OTC for weight control. Your firm is receiving this letter based on information in the Food and Drug Administration's (FDA) Drug Listing System or because you have a new drug application (NDA) or abbreviated new drug application (ANDA) for a product containing phenylpropanolamine.

This letter is to inform you of recent developments relating to phenylpropanolamine. Earlier this year, FDA received a report entitled "Phenylpropanolamine & Risk of Hemorrhagic Stroke: Final Report of the Hemorrhagic Stroke Project" from scientists at Yale University School of Medicine. This report, which is on display in Docket No. 81N-0022 in the FDA Dockets Management Branch, states that the data suggest that phenylpropanolamine increases the risk for hemorrhagic stroke.

On October 19, 2000, the Agency's Nonprescription Drugs Advisory Committee (NDAC) discussed this report and other information on phenylpropanolamine. NDAC determined that there is an association between phenylpropanolamine and hemorrhagic stroke and recommended that phenylpropanolamine not be considered generally recognized as safe for OTC use as a nasal decongestant or for weight control. 1

Based on these recent developments, FDA intends to initiate rulemaking to classify phenylpropanolamine as nonmonograph (not generally recognized as safe and effective) for OTC use. Based on the recent research findings, FDA also has significant concerns about the continued use of phenylpropanolamine in prescription drug products. FDA also intends to take action to remove phenylpropanolamine from prescription drug products. FDA plans to issue a Public Health Advisory on phenylpropanolamine to alert consumers and health professionals about the report.

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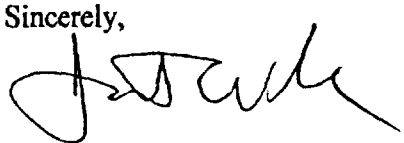
1 In the mid-1970s, phenylpropanolamine was classified as Category I (safe and effective) by two OTC drug advisory review panels. The Cough-Cold Panel's recommendations on phenylpropanolamine as a nasal decongestant appeared in the FEDERAL REGISTER of September 9, 1976 (41 FR 38312) and the Miscellaneous Internal Panel's recommendations for weight control use appeared on February 26, 1982 (47 FR 8466). However, FDA deferred its classification of phenylpropanolamine because of subsequent safety issues that were raised, pending completion of additional studies.

FDA also believes that, as an interim measure to protect the public health, you should voluntarily discontinue marketing any drug products containing phenylpropanolamine. If applicable, you may reformulate such products to remove the phenylpropanolamine ingredient.

If you have any questions or want additional information, including information about options for reformulating products that contain phenylpropanolamine, please contact Jerry Rachanow or Robert Sherman at 301-827-2241.

Your cooperation and prompt attention to this matter will be appreciated.

Sincerely,



Janet Woodcock, M.D.
Director
Center for Drug Evaluation and Research

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: JAN 18 2001

FROM: Director
Division of OTC Drug Products, HFD-560

SUBJECT: Material for Docket No. 81N-0022

TO: Dockets Management Branch, HFA-305

[X] The attached material should be placed on public display under the above referenced Docket No.

[X] This material should be cross-referenced to Comment No. CP19

Charles J. Ganley, M.D.

Attachment